

# Urinary abnormalities in non-gonococcal urethritis

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**SUMMARY** The association between urinary abnormalities detected by the two-glass urine test and objective urethritis was investigated in a study of 221 male patients with non-gonococcal urethritis. A strong correlation existed between urinary threads and urethritis, but use of the test for diagnosis and in the assessment of cure is limited by its poor predictive value in both treated and untreated patients.

## Introduction

The association of urinary abnormalities with the presence of gonococcal urethritis and non-gonococcal urethritis (NGU) is widely recognised. While the two-glass urine test is regarded by some workers<sup>1,2</sup> as only part of the assessment of a patient with symptoms suggestive of urethritis, in routine clinical practice the procedure is often used as a "test of cure" in patients without an expressible discharge after treatment.<sup>3-8</sup> Furthermore, in 10% of sexually transmitted disease (STD) clinics in England and Wales, the test is used to establish a diagnosis of NGU in the absence of urethral discharge or microscopical evidence.<sup>9</sup> The reliance that can be placed on urinary abnormalities as a means of diagnosis or of determining cure is not, however, clear. An opportunity to clarify the situation arose in a study of 221 male patients with NGU.<sup>10</sup> Each patient was assessed clinically on admission to the study and 198 patients were seen again at least once, many of them being followed for several months. On each occasion urinary abnormalities were assessed, so that we have been able to accumulate a substantial amount of data on their relationship to clinical symptoms and signs.

## Patients and methods

### SELECTION

Male patients with clinical evidence of NGU were studied, consent to undertake the work having been given by the local ethics committees. Patients

attending two clinics for sexually transmitted diseases in West London were included if the following criteria were fulfilled: (1) the patient was willing and able to give informed consent to participate in a clinical study lasting for several weeks; (2) a urethral smear contained at least 15 polymorphonuclear leucocytes per high-power microscope field (PMNL/hpf) ( $\times 800$ ) in the absence of Gram-negative intracellular diplococci, and (3) the patient had not taken antibiotics during the previous week.

### CLINICAL AND LABORATORY INVESTIGATIONS

Each patient was interviewed, and details of the nature and duration of symptoms and signs, the previous medical history, and the social and sexual background were obtained. The patient was then examined and any expressed urethral discharge Gram stained. In the absence of any urethral discharge, a sterile bacteriological loop was inserted into the urethra and material scraped from the anterior urethra was similarly stained. A second specimen was taken and either transported in Stuart's transport medium to the laboratory or plated directly on to gonococcal selective medium and incubated at 37°C in a carbon dioxide incubator for a minimum of 24 hours. Patients subsequently suspected of having, or proved to have, gonococcal infections were excluded from the study.

### Two-glass urine test

The patient was then asked to pass urine into two glasses, so that the first glass contained approximately 15 ml, and the specimens were examined for urinary abnormalities. These were defined as follows: (1) threads—of whatever type, regarded as abnormal without microscopical examination; (2) haze—any cloudiness of the urine which failed to clear on the

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addition of acetic acid; and (3) debris—any macroscopic abnormality of the urine not included in the two previous categories.

When patients returned for follow-up examination, all the investigations, except culture for *Neisseria gonorrhoeae*, were repeated.

#### SYMPTOMS

Symptoms were defined as the presence of discharge, or dysuria, or both. Pus (PMNL), in the case of follow-up specimens, was regarded as abnormal if a smear contained  $\geq 5$  PMNL/hpf.

#### TREATMENT

Patients were treated initially with minocycline or placebo and later with other tetracyclines or erythromycin.<sup>10</sup>

#### STATISTICAL METHODS

Relationships between the presence or absence of various abnormalities were analysed by the  $\chi^2$  test with Yates's correction, except that Fisher's exact test was used for all comparisons of debris in the urine of untreated patients. The relationships between urinary abnormalities and the number of PMNL/hpf (tables I and II) were analysed by the  $\chi^2$  test for linear trend. For these comparisons the overall  $\chi^2$  values on 2 degrees of freedom are also shown.

#### Results

Information on the occurrence of threads, haze, and debris in 661 urine specimens from 221 patients was available including patients initially treated with placebo. Untreated patients provided 265 specimens, and 396 were from treated patients. Three hundred and eighteen (48%) specimens were from patients with symptoms and 400 (61%) from patients with pus ( $\geq 5$  PMNL/hpf) in their urethral smear; 264 (40%) were from patients with symptoms and pus and 210 (32%) from patients with neither symptoms nor pus. There were  $\geq 15$  PMNL/hpf in the urethral smear from 277 and 5-14 PMNL/hpf in the smear from 123 patients. Threads were seen in 311 (47%), haze in 89 (13%), and debris in 31 (5%) specimens. The results for untreated and treated patients are presented separately so that the two-glass urine test can be assessed both as a diagnostic method and as a test of cure.

#### UNTREATED PATIENTS

For untreated patients (table I) there were highly significant associations between the presence of threads and symptoms, threads and pus, "at least one urinary abnormality" (largely reflecting threads)

and symptoms, and "at least one urinary abnormality" and pus. These urinary abnormalities were also significantly associated with the combination of symptoms and pus and the absence of urinary abnormalities with the absence of urethral abnormalities (symptoms or pus). There were no significant associations between haze or debris and symptoms or pus or both, either alone or in combination. Whereas the positive predictive value of a urinary abnormality for the presence of pus was high (94%, 168/179), however, the negative predictive value for the absence of pus in the absence of urinary abnormalities was low (23%, 20/86). Thus, urinary abnormalities—particularly threads—are a good indicator of the presence of urethritis, but the absence of urinary abnormalities is a bad indicator of the absence of urethritis.

#### TREATED PATIENTS

For treated patients (table II) there were significant associations between threads and pus and between "at least one urinary abnormality" and pus. The absence of threads and of "at least one abnormality" was significantly associated with the absence of symptoms and pus. There were no significant associations between symptoms, either alone or in combination with pus, and any urinary abnormality. Similarly, there were no associations between haze or debris and any combination of symptoms or pus or both. The figures for haze and debris are too small for any firm conclusion, however, except that because of their rarity they are of no great diagnostic value. In other words, the presence of a urinary abnormality was a very poor indicator of continuing urethritis (predictive value 48%, 83/174), and the absence of a urinary abnormality was a poor indicator of cure (predictive value 63%, 139/222). In only 56% (222/396) of cases was the correct diagnosis made by means of the two-glass urine test. Thus, the test is an unreliable means of determining continuing urethritis or cure in treated patients.

When urinary abnormalities were considered in relation to the severity of the urethritis, as measured by the number of PMNL/hpf (tables I and II), they were most strongly associated with the more severe urethritis in both treated and untreated patients.

#### Discussion

Since acute urethritis is a urethral inflammatory response, it is axiomatic that PMNL or pus in a urethral smear is the definitive abnormality, and to suggest that urethritis exists in its absence is illogical and can only indicate failure to obtain an adequate specimen. This may be difficult to obtain without repeated examination.<sup>11</sup> For the purpose of the present

TABLE I Association between urinary abnormalities and symptoms and signs of non-gonococcal urethritis in untreated patients

Urinary abnormalities									
Urethral abnormality	Threads			Haze			Debris		
	+	-	Significance	+	-	Significance	+	-	Significance
Symptoms	152	74	$\chi^2 = 14.9$ , P<0.001	54	172	$\chi^2 = 0.9$ NS	6	220	NS
Present	13	26		6	33		1	38	
Absent									
Pus	143	74	$\chi^2 = 13.6$ , P<0.005	53	164	$\chi^2 = 2.3$ , NS	6	211	
Present ( $\geq 15^*$ )	12	5	$\chi^2$ (for trend) = 10.7, P<0.005	3	14	$\chi^2$ (for trend) = 2.3, NS	0	17	
Absent (0-4)	10	21		4	27		1	30	
Symptoms and pus	146	66	$\chi^2 = 18.3$ , P<0.001	53	159	$\chi^2 = 2.7$ NS	5	207	NS
Present	19	34		7	46		2	51	
Absent									
Symptoms or pus	161	87	$\chi^2 = 9.9$ , P<0.01	57	191	$\chi^2 = 0.0$ NS	7	241	NS
Present	4	13		3	14		0	17	
Absent									
Total	165	100		60	205		7	258	

+ Present; - absent NS (not significant) = P&gt;0.05 \*PMNL/hpf

TABLE II Association between urinary abnormalities and symptoms and signs of non-gonococcal urethritis in treated patients

Urinary abnormalities									
Urethral abnormality	Threads			Haze			Debris		
	+	-	Significance	+	-	Significance	+	-	Significance
Symptoms	40	52	$\chi^2 = 1.9$ , NS	6	86	$\chi^2 = 0.0$ NS	5	87	NS
Present	106	198		23	281		19	285	
Absent									
Pus	30	30	$\chi^2 = 8.5$ , P<0.02	7	53	$\chi^2 = 3.9$ , NS	5	55	
Present ( $\geq 15^*$ )	44	62	$\chi^2$ (for trend) = 8.5, P<0.01	10	96	$\chi^2$ (for trend) = 3.8, NS	4	102	
Absent (0-4)	72	158		12	218		15	215	
Symptoms and pus	23	29	$\chi^2 = 1.1$ , NS	5	47	$\chi^2 = 0.2$ NS	2	50	NS
Present	123	221		24	320		22	322	
Absent									
Symptoms or pus	92	111	$\chi^2 = 12.0$ , P<0.001	17	186	$\chi^2 = 0.4$ NS	12	191	NS
Present	54	139		12	181		12	181	
Absent									
Total	146	250		29	367		24	372	

+ Present; - absent NS (not significant) = P&gt;0.05 \*PMNL/hpf

analysis, and in accordance with Bowie's criterion,<sup>12</sup> urethritis has been defined as the presence of five or more PMNL/hpf, although patients were admitted initially to the study only if  $\geq 15$  PMNL/hpf were found in their urethral smear (ie, less severe cases were omitted).

Many American physicians use an estimate of the degree of pyuria (PMNL in resuspended urinary sediment) in their diagnosis of urethritis, but British venereologists regard examination of the macroscopic appearance of urine passed into two glasses as an essential step in the assessment of a patient with symptoms or signs suggestive of urethritis. An abnormality in the first glass is regarded as evidence of anterior urethritis. If the abnormality extends to the second glass, it is believed that the disease process affects the posterior urethra.

While the two-glass test may be used with justification as part of the assessment of a patient with urethritis, to use it instead of a more direct determination of urethritis is only acceptable if the degree of association between urinary abnormalities and urethritis is so great as to make the likelihood of false-negative or false-positive results remote. Although the results of the study confirm the widely held view that urinary abnormalities are associated with the presence of urethritis, it should be noted that in an untreated patient the absence of a urinary abnormality is insufficient to exclude a diagnosis of urethritis and that in the treated patient the two-glass urine test is a poor indicator of both continuing urethritis and cure. It might be argued that because multiple specimens (range 1-9) were taken from patients, the discrepancies might have occurred only in a small group of patients with atypical findings. Equally, discrepancies may not have been found in specimens submitted by selected patients with acute urethritis of recent onset. Further analysis (unpublished data) did not confirm these suggestions. It is possible, however, that some of the discrepancies might have occurred because specimens were not taken under ideal conditions. For example, at the first visit a few patients had passed urine shortly before the tests were performed. They were instructed subsequently, however, not to pass urine for four hours before a follow-up examination. It is, therefore, unlikely that this would account for the

many patients who had urinary abnormalities in the absence of urethral pus. This study was undertaken under conditions which did not allow microscopical examination of all the threads, as is the case in many busy clinics, and it is possible that some of the threads, rather than containing PMNL, might have been mucoid in nature and therefore not related to urethritis.

We have been concerned, however, with assessing the practical use of urinary examination in the management of a patient with NGU, and the results emphasise the discrepancy between urethritis and urinary abnormalities under conditions which frequently prevail in clinics.

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